

## REMARKS

Claims 22-42 are pending. Claims 22-26, 41, and 42 are currently under examination, and claims 27-40 have been withdrawn from consideration due to a restriction requirement.

Claims 22-24 and 26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Guerret et al. (US 4,463,004; hereafter “Guerret”).

Claim 41 is rejected under 35 U.S.C. § 103 for obviousness over Guidi (*Arch. Pharm. Pharm. Med. Chem.*, 1997, 330:201-202; hereafter “Guidi”) or Guarna et al. (*Tetrahedron: Asymmetry*, 2000, 11:4227-4238; hereafter “Guarna-2000”). Claims 41 and 42 are rejected under 35 U.S.C. § 103 as being obvious in view of Guarna et al. (WO 01/64686; hereafter “Guarna-2001”), Guarna et al. (US 2003/0176414; hereafter “Guarna-2003”), Scarpi et al. (*Bioorg. Med. Chem.*, 2001, 9:1625-1632; hereafter “Scarpi”), or Machetti et al. (*Org. Lett.*, 2000, 2:3987-3990; hereafter “Machetti”). Claims 22-26 are rejected under 35 U.S.C. § 103 as being obvious in view of Guarna-2001 or Guarna-2003. Claims 22-24, 26, and 41 are rejected under 35 U.S.C. § 103 as being obvious in view of Guerret. Claims 22-26, 41, and 42 are rejected under 35 U.S.C. § 103 as being obvious in view of Guarna et al. (*J. Org. Chem.*, 1999, 64:7347-7364; hereafter “Guarna-1999”).

Claim 41 is also rejected under 35 U.S.C. § 112, first paragraph for inadequate written description.

Claims 22-26, 41, and 42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of co-pending Application No. 10/220,556 (published as US 2003/0176414; hereafter “the ‘556 application”).

The rejections are addressed below.

### Amendments to the Claims

Claim 22 has been amended to recite compounds of formula (I) in which X is O and R<sub>1</sub> is H. The remaining claims have been amended for consistency with claim 22. No new matter has been added.

### Rejections Under 35 U.S.C. § 112, first paragraph

The Office has rejected claim 41 for lack of adequate written description for various substituents previously recited in the proviso clause of the claim. This claim has been cancelled, and the rejection is now moot.

### Rejections Under 35 U.S.C. § 102(b)

Claims 22-24, and 26 are rejected for anticipation by Guerret. The Examiner asserts that, in claim 1 and Table I, Guerret teaches many compounds of formula (I), wherein X is H, Y and Z are O, R<sub>2</sub>, R<sub>4</sub>, R<sub>5</sub>, and R<sub>6</sub> are H, R<sub>1</sub> is H, alkyl having at least 4 carbons, cyclohexyl, or aryl, and R<sub>3</sub> is C<sub>1</sub> to C<sub>4</sub> alkyl, cyclohexyl, or benzyl. Applicants have amended claim 22, from which claims 23, 24, and 26 depend, to be limited to compounds of formula (I) in which X is O and R<sub>1</sub> is H. These compounds are not anticipated by Guerret. Applicants respectfully request that this rejection be withdrawn.

### Rejections Under 35 U.S.C. § 103

#### *Guidi*

Claim 41 is rejected under 35 U.S.C. § 103 for obviousness over Guidi. This claim has been cancelled, and this rejection is now moot.

*Guerret*

Claims 22-24, 26, and 41 are rejected for obviousness over Guerret. The Examiner asserts that, in claim 1 and Table I, Guerret teaches the compound of formula (I) wherein X is H, Y and Z are O, R<sub>2</sub>, R<sub>4</sub>, R<sub>5</sub>, and R<sub>6</sub> are H, R<sub>1</sub> is H, alkyl having at least 4 carbons, cyclohexyl, or aryl, and R<sub>3</sub> is C<sub>1</sub> to C<sub>4</sub> alkyl, cyclohexyl, or benzyl. As stated above, the rejected claims are now limited to compounds of formula (I) wherein X is O and R<sub>1</sub> is H. Accordingly, the compounds of formula (I) are not adjacent homologs to the compounds disclosed in Guerret, and the rejection may be withdrawn.

*Guarna-2001 and Guarna-2003*

Claims 22-26, 41 and 42 are rejected for obviousness in view of Guarna-2001 and Guarna-2003, which is the US National Stage of Guarna-2001. The Examiner asserts that, in compound 214, Guarna-2001 and Guarna-2003 teach the instant compounds 138 and 142 with undefined stereochemistry such that it would have been obvious to resolve the stereoisomers having substantially different pharmacological activity. The instant claims have been amended to require that X be O and R<sub>1</sub> be H. In contrast, X is H and R<sub>1</sub> is 4-OH-Ph for compound 214 of Guarna-2001 and Guarna-2003. Thus, the compounds of formula (I) presently claimed are not stereoisomers of compound 214 of Guarna-2001 and Guarna-2003, and the rejection may be withdrawn.

*Guarna-2000*

Claim 41 is rejected for obviousness in view of Guarna-2000. As discussed, this claim has been cancelled, and the rejection may be withdrawn.

*Scarpi*

Claims 41 and 42 are rejected for obviousness in view of Scarpi. The Examiner asserts that, in compound 1 on page 1627, Scarpi teaches compound 32 of formula (I), as defined in claim 25, such that making compound 33 of formula (I), as defined in claim 25, which is a stereoisomer of compound 32, is obvious. Claim 41 has been cancelled, and claim 42 has been amended to delete reference to compound 33. This rejection may also be withdrawn.

*Machetti*

Claims 41 and 42 are rejected for obviousness in view of Machetti. The Examiner asserts that, in compound 1 on page 1627, Machetti teaches compound 36 of formula (I), as defined in claim 25, such that the preparation of compound 37 of formula (I), as defined in claim 25, which is a stereoisomer of compound 36, is obvious. Again, claim 41 has been cancelled, and claim 42 has been amended to delete reference to claim 37. This rejection may also be withdrawn.

*Guarna-1999*

Claims 22-26, 41, and 42 are rejected for obviousness in view of Guarna-1999. The Examiner asserts that, Guarna-1999 teaches compounds comprising the 3-aza-bicyclo[3.2.1]octane core including specific exemplary compounds. As discussed, the present claims have now been amended to require that X be O. Accordingly, the claimed compounds are

3-aza-2-*oxo*-6,8-dioxabicyclo[3.2.1]octanes (BTAa(O)) (see Scheme 1 of Guarna-1999).

Guarna-1999 only teaches that the BTAa(O) compounds are starting materials for use in synthesizing the desired BTAa compounds (see page 7347, 2<sup>nd</sup> col.).

With respect to claims 22-26, Applicants maintain that Guarna-1999 fails to teach or suggest a specific pharmaceutical utility for any of the disclosed compounds. In addition, the comments relied on by the Office to support its assertion of a pharmaceutical utility relate only to the BTAa compounds and not to the disclosed BTAa(O) compounds, i.e., compounds where X=O. For example, the Abstract states: “the BTAa compounds [are] potential dipeptide isosteres useful for the synthesis of modified peptides.” Thus, even assuming the Office’s assertions with respect to the BTAa compounds are correct (which Applicants do not conceded), Guarna-1999 still teaches no pharmaceutical utility for 3-aza-2-*oxo*-6,8-dioxabicyclo[3.2.1]octanes, and the disclosure of any such compound in Guarna-1999 does not render the pharmaceutical compositions of claims 22-26 obvious.

For claims 41 and 42, the Examiner has also asserted that Guarna-1999 discloses compound 192 and that this disclosure renders compounds 193-195 obvious. Claim 41 has been cancelled, and claim 42 has been amended to delete reference to compounds 193-195. This rejection may also be withdrawn.

#### Provisional Obviousness-Type Double Patenting Rejection

Claims 22-26, 41, and 42 are provisionally rejected for non-statutory obviousness-type double patenting over claims 1-5 of U.S. Serial No. 10/220,556. Applicants respectfully disagree with this provisional rejection, because the claims of the present application and those of the ‘556 application are not identical, as acknowledged by the Examiner, and the claims are patentably

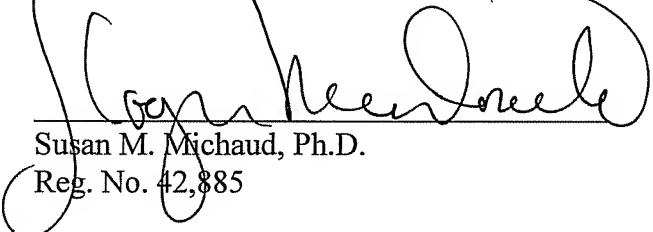
distinct for the same reasons provided above in response to the Examiner's rejections of the claims for obviousness in view of Guarna-2003, which is a corresponding publication of the '556 application. Applicants thus respectfully request that this rejection be withdrawn.

### CONCLUSION

Applicants submit that the amended claims are in condition for allowance, and this action is respectfully requested. Enclosed are a Petition to extend the period for replying to the Office action for three months, to and including November 29, 2007, and a check in payment of the required extension fee. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: October 30, 2007



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